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CLAIMS:

1. An opioid compound of general formula I

[opioid-N]-[spacer]-[charged group],

I

in which an opioid compound is linked via the nitrogen at position 17 to a spacer group, which in turn is linked to a charged group,

or a pharmaceutically acceptable salt thereof.

2. A compound according to Claim 1, in which the spacer is a straight or branched alkyl, alkenyl or alkenyl chain of 1 to 6 carbon atoms, which may optionally be substituted.

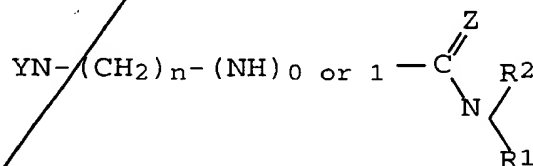
3. A compound according to Claim 1, in which the spacer is a cyclic alkyl, alkenyl or alkynyl group, which may optionally be substituted.

4. A compound according to any one of Claims 1 to 3, in which the spacer group is unsubstituted.

5. A compound according to any one of Claims 1 to 4, in which the spacer group is of 2 to 3 carbon atoms.

6. A compound according to any one of Claims 1 to 5, in which the charged group is an amidine or guanidine group.

7. A compound according to Claim 1, of general formula (II)



in which

YN- represents an organic residue obtained by removal of the R group from an opioid compound of general formula

(IIIa)

or of the general formula

1

 \mathbb{R}^4

(II Ib)

Z is O, S or NR³;

R² is H or an alkyl group having 1 to 6 carbon

n is an integer of 1 to 6,

~~R¹ and R³ may together complete an addition ring,
or a pharmaceutically acceptable salt thereof.~~

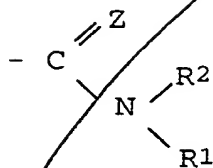
8. A compound according to Claim 7, in which R^1 and R^3 together complete an addition ring, and the grouping

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Cont

Year	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100																																																																																																																																																																																																
Population (millions)	1.2	1.3	1.4	1.5	1.6	1.7	1.8	1.9	2.0	2.1	2.2	2.3	2.4	2.5	2.6	2.7	2.8	2.9	3.0	3.1	3.2	3.3	3.4	3.5	3.6	3.7	3.8	3.9	4.0	4.1	4.2	4.3	4.4	4.5	4.6	4.7	4.8	4.9	5.0	5.1	5.2	5.3	5.4	5.5	5.6	5.7	5.8	5.9	6.0	6.1	6.2	6.3	6.4	6.5	6.6	6.7	6.8	6.9	7.0	7.1	7.2	7.3	7.4	7.5	7.6	7.7	7.8	7.9	8.0	8.1	8.2	8.3	8.4	8.5	8.6	8.7	8.8	8.9	9.0	9.1	9.2	9.3	9.4	9.5	9.6	9.7	9.8	9.9	10.0	10.1	10.2	10.3	10.4	10.5	10.6	10.7	10.8	10.9	11.0	11.1	11.2	11.3	11.4	11.5	11.6	11.7	11.8	11.9	12.0	12.1	12.2	12.3	12.4	12.5	12.6	12.7	12.8	12.9	13.0	13.1	13.2	13.3	13.4	13.5	13.6	13.7	13.8	13.9	14.0	14.1	14.2	14.3	14.4	14.5	14.6	14.7	14.8	14.9	15.0	15.1	15.2	15.3	15.4	15.5	15.6	15.7	15.8	15.9	16.0	16.1	16.2	16.3	16.4	16.5	16.6	16.7	16.8	16.9	17.0	17.1	17.2	17.3	17.4	17.5	17.6	17.7	17.8	17.9	18.0	18.1	18.2	18.3	18.4	18.5	18.6	18.7	18.8	18.9	19.0	19.1	19.2	19.3	19.4	19.5	19.6	19.7	19.8	19.9	20.0	20.1	20.2	20.3	20.4	20.5	20.6	20.7	20.8	20.9	21.0	21.1	21.2	21.3	21.4	21.5	21.6	21.7	21.8	21.9	22.0	22.1	22.2	22.3	22.4	22.5	22.6	22.7	22.8	22.9	23.0	23.1	23.2	23.3	23.4	23.5	23.6	23.7	23.8	23.9	24.0	24.1	24.2	24.3	24.4	24.5	24.6	24.7	24.8	24.9	25.0	25.1	25.2	25.3	25.4	25.5	25.6	25.7	25.8	25.9	26.0	26.1	26.2	26.3	26.4	26.5	26.6	26.7	26.8	26.9	27.0	27.1	27.2	27.3	27.4	27.5	27.6	27.7	27.8	27.9	28.0	28.1	28.2	28.3	28.4	28.5	28.6	28.7	28.8	28.9	29.0	29.1	29.2	29.3	29.4	29.5	29.6	29.7	29.8	29.9	30.0	30.1	30.2	30.3	30.4	30.5	30.6	30.7	30.8	30.9	31.0	31.1	31.2	31.3	31.4

Sub

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~~forms a heterocyclic moiety.~~

9. A compound according to Claim 8, in which the heterocyclic moiety is a 2-imidazolyl or 2-imidazolinyll group of formula:



10. A compound according to Claim 8 or Claim 9, in which R is CH₃.
11. A compound according to any one of Claims 8 to 10, in which n is 2 or 3.
12. A compound according to any one of Claims 8 to 11, in which Z is NH, and R¹ and R² are both H.
13. A compound according to any one of Claims 8 to 11, in which the precursor of YN- or Y¹NR⁴- is a compound selected from the group consisting of morphine, codeine, heroin, ethylmorphine, O-carboxymethylmorphine, O-acetylmorphine, hydrocodone, hydromorphone, oxycodone, dihydrocodeine, thebaine, metopon, etorphine, acetorphine, ketobemidone, ethoheptazine, diprenorphine (M5050), buprenorphine, phenomorphan, levorphanol, pentazocine, eptazocine and metazocine.
14. A compound according to Claim 13, in which the precursor of YN- or Y¹NR⁴- is morphine, codeine or buprenorphine.
15. A compound according to Claim 1, in which the opioid compound of formula (IIIa) or (IIIc) is selected from the group set out in Table 1.

16. A compound according to Claim 1, in which the compound of general formula I is selected from the group consisting of KRS-41, KRS-2-19, KRS-3-7, KRS-3-23-4, KRS-3-28, KRS-3-30-2, KRS-3-56, KRS-2-63, KRS-4-8, and KRS-2-47, as herein defined.

17. An opiate receptor agonist having analgesic properties and having reduced or no CNS activity, of general formula I or general formula II as defined in any one of claims 1 to 16.

18. A method of reducing the central nervous system activity of an opioid compound, comprising the step of linking the nitrogen atom at position 17 of said compound to a spacer group, which in turn is linked to a charged group, optionally via a spacer group.

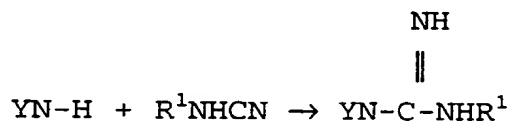
19. A method for the preparation of a compound of formula II as defined in any one of Claims 8 to 14, in which YN- may be replaced by Y¹NR⁴-, comprising the steps of

(a) Reaction of a compound of formula



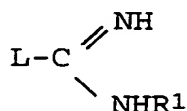
(IV)

with a cyanamide, R¹NHCN, according to the equation



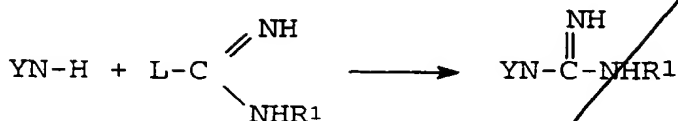
or

(b) Reaction of a compound of formula (IV) with a compound of formula



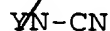
(V)

wherein L is a leaving group, according to the equation



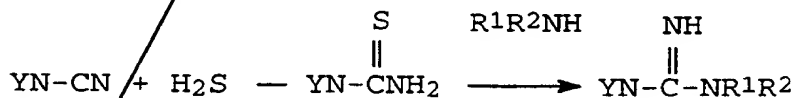
20. A method for the preparation of a compound of formula II as defined in any one of Claims 8 to 14 in which Z is NR^2 , comprising the steps of

(a) Reaction of a compound of the formula



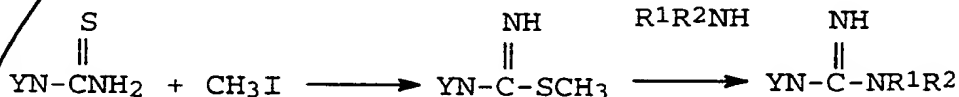
(VI)

with H_2S to obtain an N-thiocarboxamide YN-CSNH_2 , which is reacted with an amine $\text{R}^1\text{R}^2\text{NH}$ according to the two-stage equation



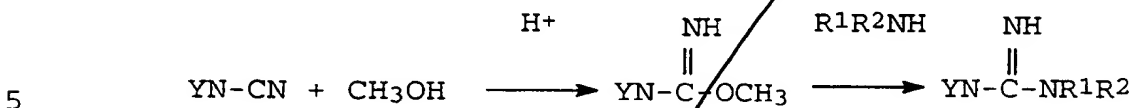
to yield compounds of the invention where Z is S and where Z is NH, or

(b) Methylating the N-thiocarboxamide to yield an isothiourea compound, which is in turn reacted with an amine $\text{R}^1\text{R}^2\text{NH}$:

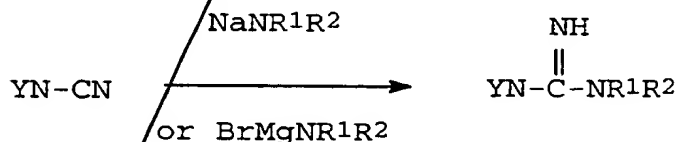


21. A method of synthesis of a compounds of formula (II) as defined in any one of Claims 8 to 14, comprising the step of reacting an N-cyano compound of

formula (VI) as defined in Claim 19 with methanol under acidic conditions to yield an isourea, which in turn is reacted with an amine according to the equation



22. A method of synthesis of a compound of formula (II) as defined in any one of Claims 8 to 13 in which Z is N, comprising the step of reacting an N-cyano compound of formula (VI) as defined in Claim 19, and a metallated residue
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23. A composition comprising a compound according to any one of Claims 1 to 16, together with a pharmaceutically acceptable carrier.
24. A method of inducing analgesia, comprising the step of administering an effective amount of a compound according to any one of Claims 1 to 16 to a mammal in need of such treatment.
25. A method according to Claim 23 in which the mammal is a human.
26. Use of a compound according to any one of Claims 1 to 16 in medicine.
27. Use of a compound according to any one of Claims 1 to 16 for the manufacture of a medicament for inducing analgesia.